UNITED STATES PATENT AND TRADEMARK OFFICE

T

UNITED STATES DEPARTMENT OF COMMERCE
United States Patent and Trademark Office
Address: COMMISSIONER FOR PATENTS
P.O. Box 1450
Alexandria, Virginia 22313-1450
www.uspto.gov

APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/865,420	05/29/2001	Mitsuru Ohkubo	205625US0CONT	6383

22850 7590 05/16/2006

OBLON, SPIVAK, MCCLELLAND, MAIER & NEUSTADT, P.C.
1940 DUKE STREET
ALEXANDRIA, VA 22314

EXAMINER	
ROBINSON, BINTA M	
ART UNIT	PAPER NUMBER
1625	

DATE MAILED: 05/16/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/865,420	OHKUBO ET AL.	
	Examiner	Art Unit	
	Binta M. Robinson	1625	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-14,16-22,25-27 and 29-47* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☒ Claim(s) *7,9,12 and 29* is/are allowed.

6)☒ Claim(s) *1,2,13,14,16-19,22,30-42 and 44-47* is/are rejected.

7)☒ Claim(s) *3-6,8,10, 11, 20-21, 25-27, 43* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☒ Certified copies of the priority documents have been received in Application No. 08/495,572.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

Detailed Action

The 112, first paragraph rejections of claims 23-24, the objection to claims 39-41, the 112, second paragraph rejection of claims 23-24, 39, 40-41, the statutory double patenting rejection of claim 20, the obvious double patenting rejections of claims 1-20, 23-29, 39-47 are rendered moot in light of applicant's remarks filed 1/13/05 and due to the approval of applicant's terminal disclaimer filed 1/13/05.

(objections)

Applicant is advised that should claim 41 be found allowable, claim 39 will be objected to under 37 CFR 1.75 as being a substantial duplicate thereof. When two claims in an application are duplicates or else are so close in content that they both cover the same thing, despite a slight difference in wording, it is proper after allowing one claim to object to the other as being a substantial duplicate of the allowed claim. See MPEP § 706.03(k).

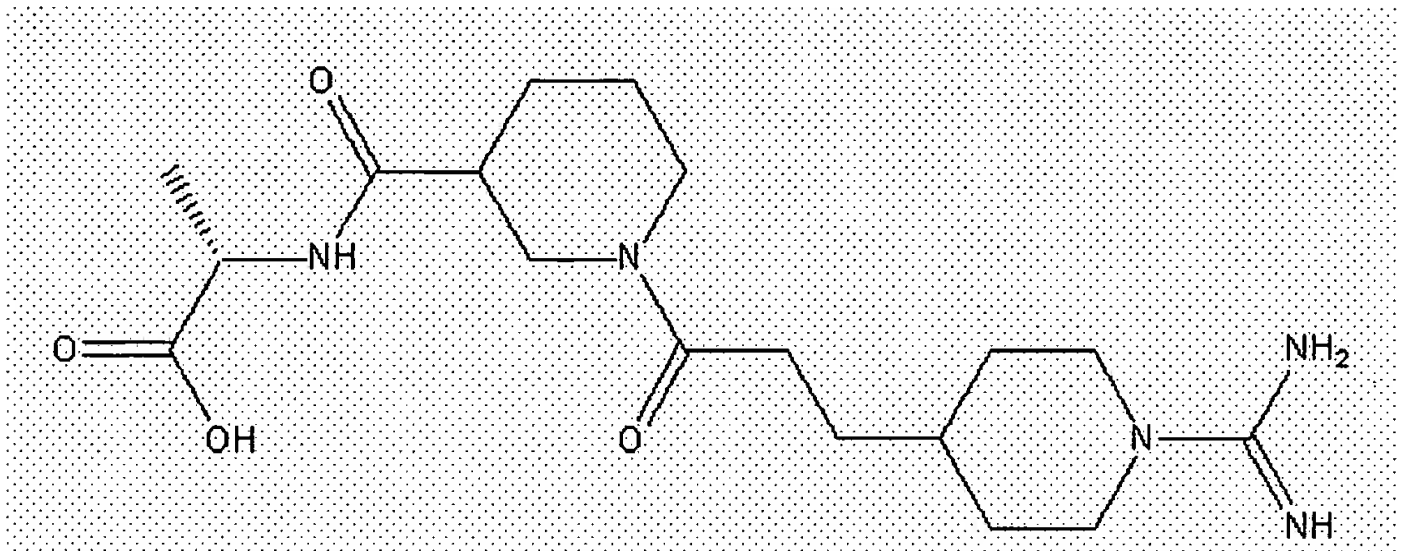
(new rejections)

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

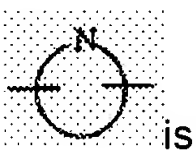
> A person shall be entitled to a patent unless --
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claim(s) 1, 2, 14, 16, 17, 18, 19, 22, 39, 40, 41, 42, and 44 are rejected under 35 U.S.C. 102(b) as being anticipated by Alig et. al. (See Reference A). Alig et. al.

discloses the instant compound,



n-[[1-{3-(1-amidino-4-piperidinyl)propionyl}-3-piperidinyl]carbonyl]-alanine which

anticipates the instant compound because in the Alig compound, R2 is carboxyl, A3 is a methylene group substituted with a methyl group, Z is NHC(O), R3 is H,  is 3-piperidinyl, A1 is ethylene, R1 is 4-piperidinyl, and the amidino moiety is the substitution on the N-containing cycloalkyl which is R1 ; the method of producing medicaments containing the Alig compound in the form of tablets, film tablets, coated tablets, hard and soft gelatin capsules, solutions, emulsions, or suspensions; and a method of preventing in particular the formation of blood platelet thrombi, and the treatment of diseases such as thrombosis, cerebral infarct, myocardial infarct, inflammation and arteriosclerosis. At column 28, lines 63-64, see the instant compound, at column 8, see the instant method of preparing this medicament, and at column 7, lines 55-68, see the instant method of treating these diseases with the instant compound.

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to

> enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

Claim 17 is rejected under 35 U.S.C. 112, first paragraph, because the specification, does not reasonably provide enablement for treating the any of the diseases in claim 17. The specification does not enable any physician skilled in the art of medicine, to make the invention commensurate in scope with these claims. The how to make requirement of the enablement statute, when applied to process claims, refers to operability and how to make the claimed process work. "The factors to be considered [in making an enablement rejection] have been summarized as the quantity of experimentation necessary, the amount of direction or guidance presented, the presence or absence of working examples, the nature of the invention, the state of the prior art, the relative skill of those in that art, the predictability or unpredictability of the art and the breadth of the claims", *In re Rainer*, 146 USPQ 218 (1965); *In re Colianni*, 195 USPQ 150, *Ex parte Formal*, 230 USPQ 546. The four main issues are the correlation between clinical efficacy for disease treatment and Applicants' single and lone in vitro assay.

a) Determining if any particular claimed compound would treat any particular disease caused by thrombus formation would require synthesis of the compound, formulation into a suitable dosage form, and subjecting it clinical trials with a number of fundamentally different diseases described below, or to testing them in an assay known to be correlated to clinical efficacy of such treatment. This is a large quantity of experimentation. b) The direction concerning treating the thrombus formation diseases is

found in the passage spanning line 26, page 1, through line 16, page 2, which merely states Applicants' intention to do so. Applicants describe formulations in line 19, page 48 through line 2, page 49. Doses required to practice their invention are described in line 24, page 49 through line 1 page 50. A 10,000-fold range of doses is recommended. There are no guidelines for determining the doses needed to provide an adjuvant therapy effect *vs.* a transplantation effect *vs.* an anti-restenosis effect. Are the identical doses to be used for treating these unrelated diseases? There is an *in vitro* assay described in line 31, page 47 through line 18, page 48 with data on one single compound but it is unclear if this assay is correlated to clinical effectiveness of treating diseases. c) There is no working example of treatment of any disease in man or animals. d) The nature of the invention is clinical treatment of disease with inhibitors of the platelet aggregation, which involves physiological activity. e) The state of the clinical arts in platelet aggregation-related diseases is individual antiplatelet agents have become standard in both the prevention and treatment of conditions such as MI, Stroke, and unstable angina. (See McNicol et. al., page 391, last paragraph). However, the recent experience with oral αIIβ3 Integrin antagonists and thromboxane receptor antagonists cautions that modulation of platelet interactions with other components of the vascular system can have unforeseen consequences.

(See McNicol et. al., page 391, last paragraph)

f) The artisan using Applicants invention would be a physician with a MD degree and several years of experience. g) It is well established that "the scope of enablement

varies inversely with the degree of unpredictability of the factors involved", and physiological activity is generally considered to be an unpredictable factor. See *In re Fisher*, 166 USPQ 18, at 24 (In cases involving unpredictable factors, such as most chemical reactions and physiological activity, the scope of enablement obviously varies inversely with the degree of unpredictability of the factors involved.), *Nationwide Chemical Corporation, et al. v. Wright, et al.*, 192 USPQ 95 (one skilled in chemical and biological arts cannot always reasonably predict how different chemical compounds and elements might behave under varying circumstances), *Ex parte Sudilovsky* 21 USPQ2d 1702 (Appellant's invention concerns pharmaceutical activity. Because there is no evidence of record of analogous activity for similar compounds, the art is relatively unpredictable) *In re Wright* 27 USPQ2d 1510 (the physiological activity of RNA viruses was sufficiently unpredictable that success in developing specific avian recombinant virus vaccine was uncertain). h) The scope of the claims involves all of the billions of compounds of claim 1 as well as the hundred of diseases embraced by the term "diseases caused by thrombus formation" . Thus, the scope of claims is enormous.

MPEP §2164.01(a) states, "A conclusion of lack of enablement means that, based on the evidence regarding each of the above factors, the specification, at the time the application was filed, would not have taught one skilled in the art how to make and/or use the full scope of the claimed invention without undue experimentation. *In re Wright*, 999 F.2d 1557,1562, 27 USPQ2d 1510, 1513 (Fed. Cir. 1993)." That conclusion is clearly

justified here and undue experimentation will be required to practice Applicants' invention.

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter, which the applicant regards as his invention.

Claims 13, 30, 31, 32, 33, 34, 35, 36, 37, 38, 39, 40, 45, 46, 47 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 39, 40, 45, and 46 are indefinite and are rejected because they are pharmaceutical compositions claims that do not recite a pharmaceutically acceptable carrier.

B. In claim 47, the term "purified" is unclear. How purified is the claimed compound?

C. In claim 13, line 8, page 10, and everywhere else throughout the claim and in claims 30, 31, 32, 33, 34, 35, 36, 37, 38 the phrase "defined above" is unclear. Does the applicant mean that the radicals are defined at the claim or in preceding claims?

Claims 7, 9, 12, 29 are allowable.

Claims 25-27, 42 are objected to for being based on a rejected claim.

Claim 21 is objected to as being dependent upon a rejected base claim, but would be allowable if rewritten in independent form including all of the limitations of the base claim and any intervening claims.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Binta M. Robinson whose telephone number is (571) 272-0692. The examiner can normally be reached on M-F (9:30-6:00).

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dr. Thomas Mckenzie can be reached on 571-272-0670.

A facsimile center has been established. The hours of operation are Monday through Friday, 8:45 AM to 4:45 PM. The telecopier numbers for accessing the facsimile machine are (703)308-4242, (703)305-3592, and (703)305-3014.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (571)-272-1600.

BMR
May 12, 2006

Thomas McKenzie
SPE
AU 1624